

MULTICENTRIC RETICULOHISTIOCYTOSIS- A RARE AND DISABLING DISEASE

OMOWUNMI ASHAOLU¹, Selwyn Ng¹, Shaun Smale¹, and Jenny Hughes¹

¹Princess of Wales Hospital

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Omowunmi Ashaolu¹, Selwyn Ng², Shaun Smale³, Jenny Hughes¹

¹Clinical fellow, Department of Dermatology, Princess of Wales Hospital, Bridgend, UK, wunmi.ashaolu@wales.nhs.uk

²Consultant, Department of Histopathology, Morriston Hospital, Swansea, UK, selwyn.ng@wales.nhs.uk

³Consultant, Department of Rheumatology, Princess of Wales Hospital, Bridgend UK, shaun.smale@wales.nhs.uk

¹Consultant, Department of Dermatology, Princess of Wales Hospital, Bridgend, UK, jenny.hughes@wales.nhs.uk.

A 39-year-old man presented with 5-week history of multiple discrete and skin-coloured lesions on his hands, forearms, and face. He also had severely painful, stiff, and swollen fingers. He was otherwise well with no relevant personal or family history. Skin examination showed multiple discrete and coalescing firm, reddish brown, tender papules of varying sizes distributed mainly over the dorsum of the hands and nail folds (Fig 1) with no mucosal involvement. There was bilateral swelling and stiffness of the joints, especially the distal interphalangeal joints.

Baseline investigations, autoantibody, viral screen, and staging CT to rule out underlying malignancy were normal. Radiographs of both hands showed soft tissue swelling and subtle periosteal reactions in the small joints of the hands. Histopathology of the skin biopsy showed infiltration of the dermis and subcutaneous fat by mononuclear and multinucleated histiocytes with granular eosinophilic cytoplasm that showed positivity for CD45, CD68 and factor 13a and negativity for S100- and CD1a (Fig 2). Based on these findings a diagnosis of multicentric reticulohistiocytosis was made.

He was initially treated with non-steroidal anti-inflammatory, Morphine, Alendronate and Oral corticosteroids. With worsening disease activity, Denosumab, oral methotrexate, hydroxychloroquine, infliximab, tocilizumab and leflunomide were added sequentially, however there was no symptom improvement. He was then considered for Tofacitinib 5mg twice daily with improvement after 4 weeks of initiating this therapy evidenced by improved sleep, skin symptoms and joint pains.

Multicentric reticulohistiocytosis is a rare, multisystem inflammatory disease with unknown aetiology. It was first reported by Weber and Freudenthal in 1937, however Goltz and Laymon coined the term multicentric reticulohistiocytosis in 1954. Approximately 300 cases have been reported in the literature with most from Europe and United States. It is slightly predominant in women¹ and symptoms manifest from the fourth decade of life². Associated involvement of the joints impacts significantly on patients' quality of life due

to limitations on activities of daily living which inadvertently increases the risk of increased anxiety and depression.

The cause of MRH is not known but activated macrophages and increased levels of TNF-alpha, IL-12, IL-1, and IL-6³ have been documented.

Cutaneous manifestation of MRH includes firm, discrete clustered reddish brown to flesh-coloured papules or nodules that gradually enlarge in size. It typically occurs over the joints of fingers and wrists giving a characteristic coral bead appearance¹ as seen in our patient. Other commonly affected include the face giving leonine facies. However any part of the body can be affected including nail⁴, mucosal surfaces¹, lungs and heart. Fever, weight loss and malaise have also been reported. In addition, symmetrical polyarthritis mainly affecting the hands can potentially progress to arthritis mutilans. Differential diagnosis includes rheumatoid arthritis and psoriatic arthritis.

Although MRH is not a paraneoplastic disease, solid organ especially breast and stomach carcinomas and haematological malignancies have been reported in 31% of cases⁵ therefore underlying malignancy should always be ruled out in a patient with MRH.

There is no laboratory test specific for MRH. Histological studies show multinucleated giant cells with pale, fine, granular eosinophilic cytoplasm in the dermis. Stains are negative for S100, CD34, factor XIIIa and alpha-1-antitrypsin but positive for PAS and histiocytes (vimentin, CD68, CD45 and MAC387)². Langerhans granules are absent on electron microscopy.

There are no established treatment guidelines owing to the rarity and lack of controlled studies of the disease. The disease can be self-limiting, however this may have caused severe joint destruction. Prednisolone, immunomodulatory and disease modifying antirheumatic drugs, TNF inhibitors either as monotherapies or combination therapies have shown varying response. Tofacitinib, a selective JAK inhibitor, licenced for the treatment of rheumatoid arthritis has also been reported to be of benefit in the treatment of MRH⁶.

MRH is a rare disease that cause disfiguring skin lesions and disabling arthritis therefore early recognition, and treatment is important to prevent long term deformities. In conclusion, we present a patient with a very rare non-Langerhans cell histiocytosis with typical clinical, histopathological and immunohistochemical findings.

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Fig 1: Showing coral bead appearance of multicentric reticulohistiocytosis

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Fig 2: Immunohistological pictures:(a) Dense diffuse dermal infiltrate consisting of large histiocytes and multinucleated giant cells showing eosinophilic ‘ground glass appearance’;(b) diastase resistant granules in the cytoplasm (c) Positive CD68 immunohistochemical stain (brown colour) in the macrophages (d) Positive CD45 immunohistochemical stain (brown colour) in the macrophages

Author contributions

Author 1-Omowunmi Ashaolu- Writing-original draft preparation, review and editing.

Author 2- Shaun Smale- Review and approval

Author 3- Selwyn Ng- Review and approval

Author 4- Jenny Hughes- Conceptualization, Supervision, Review and Editing

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